Cardiovascular control during concomitant dynamic leg exercise and static arm exercise in humans

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1. Skeletal muscle blood flow is thought to be determined by a balance between sympathetic vasoconstriction and metabolic vasodilatation. The purpose of this study was to assess the importance of high levels of sympathetic vasoconstrictor activity in control of blood flow to human skeletal muscle during dynamic exercise.

2. Muscle sympathetic nerve activity to the exercising leg was increased by static or static ischaemic arm exercise added to on-going dynamic leg exercise. Ten subjects performed light (20 W) or moderate (40 W) dynamic knee extension for 6 min with one leg alone or concomitant with bilateral static handgrip at 20% of maximal voluntary contraction force with or without forearm muscle ischaemia or post-exercise forearm muscle ischaemia.

3. Muscle sympathetic nerve activity was measured by microneurography (peroneal nerve) and leg muscle blood flow by a constant infusion thermodilution technique (femoral vein).

4. Activation of an exercise pressor reflex from the arms, causing a 2- to 4-fold increase in muscle sympathetic nerve activity and a 15–32% increase in mean arterial blood pressure, did not affect blood flow to the dynamically exercising leg muscles at any level of leg exercise. Leg vascular conductance was reduced in line with the higher perfusion pressure.

5. The results demonstrate that the vasoconstrictor effects of high levels of muscle sympathetic nerve activity does not affect blood flow to human skeletal muscle exercising at moderate intensities. One question remaining is whether the observed decrease in muscle vascular conductance is the result of sympathetic vasoconstriction or metabolic autoregulation of muscle blood flow.

Since the development of the microneurographic technique for measuring muscle sympathetic nerve activity (MSNA) in humans, several studies have demonstrated an increase in sympathetic outflow to skeletal muscle during static muscle contractions (Mark *et al.* 1985; Wallin *et al.* 1989; Saito *et al.* 1990; Hansen *et al.* 1994; Kagaya *et al.* 1994). The increase in MSNA is associated with an increase in arterial blood pressure, heart rate and cardiac output and is attributed to a reflex arising in the contracting muscles where chemical changes activate thin nerve fibre afferents (also termed the metaboreflex) (Mitchell, 1985; Kaufman & Rybicki, 1987; Victor *et al.* 1989) and to the neural drive associated with motor command signals projecting to the vasomotor circuits in the brainstem, termed central command (Eldridge *et al.* 1985). The functional significance of the metaboreflex has been debated since the early work of Alam & Smirk (1937), who proposed that the afferent arm of the reflex signals a mismatch between muscle oxygen delivery and utilization and that the efferent response evoking an increase in arterial blood pressure serves to correct this by increasing muscle perfusion pressure and thereby muscle blood flow.

The effects of an increase in MSNA on active skeletal muscle haemodynamics is still a major subject of discussion. Donald & Ferguson (1970) and Thompson & Mohrman (1983) showed that electrical stimulation of the sympathetic nerves to the dog hindlimb caused similar percentage reductions in muscle blood flow at rest and during the most severe exercise. However, in the same dogs (Donald *et al.* 1970), acute ablation of the sympathetic nerve supply to exercising hindlimbs was without effect on blood flow at any level of exercise, indicating that in this animal there is no tonic restraint of blood flow to active muscles. Remensnyder *et al.* (1962) concluded that the vascular response to maximal stimulation of the sympathetic nerves in dogs was markedly reduced with increasing exercise intensity.

In man the question of sympathetic vasoconstriction in active muscle is important for the understanding of cardiovascular control during heavy dynamic exercise with a large muscle mass. Several authors have proposed that sympathetic vasoconstriction limits active muscle blood flow in situations where the theoretical total blood flow requirements exceed the maximal cardiac output (Andersen & Saltin, 1985), but

Table 1. Exercise protocol 1

Arm ischaemia	—	—	—	—	+	+	—	—	—	—	—	+ +
Arm work, 20 % MVC	—	—	+	—	+	—	—	—	—	+	—	+ —
Leg work (W)	20	—	20	—	20	20	—	40	—	40	—	40 40
Minutes	6	15	6	15	6	3	30	6	15	6	15	6 3

clear evidence for this is still missing (Secher *et al.* 1977; Savard *et al.* 1989; Strange *et al.* 1990; Pawelczyk *et al.* 1992; Richter *et al.* 1992; Richardson *et al.* 1995).

The haemodynamic consequences of manoeuvres activating the metaboreflex and increasing muscle sympathetic nerve activity have been studied in man in both resting and exercising muscle. In resting calf muscle increased MSNA causes a reduction in muscle vascular conductance (Seals, 1989; Jacobsen *et al.* 1994) and in some cases also a reduction in muscle blood flow (Saito *et al.* 1990). In dynamically exercising muscle concomitant static handgrip exercise causes a reduction in muscle vascular conductance (Kilbom & Brundin, 1976; Sinoway *et al.* 1989) and – in two studies by Kagaya *et al.* – also a reduction of muscle blood flow during intermittent plantar flexion at very low intensity (Kagaya, 1993; Kagaya *et al.* 1994). In other studies activation of the muscle chemoreflex has reduced muscle vascular conductance but increased muscle blood flow (Mittelstadt *et al.* 1994). In one study, post-exercise muscle ischaemia in one leg caused an increase in flow and vascular conductance in the opposite dynamically exercising leg (R. Boushel, P. Madson, H. B. Nielsen & N. H. Secher, personal communication).

The aim of the present study was to investigate whether powerful muscle chemoreflex activation will reduce blood flow to the knee extensor muscles of one leg exercising at moderate intensities. Graded muscle chemoreflex activation was accomplished by exhaustive static handgrip with both arms for several minutes with and without occlusion of forearm blood supply.

METHODS

Ten men, aged 22 to 27 years, volunteered as subjects, and after being fully informed, gave written consent to participate. The study was approved by the Copenhagen Ethics Committee. All subjects were physically active students in good health.

Subjects came to the laboratory at 08.00 h after a light breakfast. Femoral arterial and venous catheters as well as a central venous catheter were inserted and the subjects were allowed to rest for 1 h. The studies were performed 2 h post prandially. Dynamic leg exercise was performed as knee extension with one leg on a modified Krogh cycle ergometer (Andersen *et al.* 1985). The subjects were placed sitting on the ergometer. A rod attached to the ankle and the crank of the ergometer was used to transfer movement of the lower leg to the cycle. The work rate was controlled by a weight balance system. Dynamic knee extension was performed at a rate of 60 contractions per minute, with each contraction causing the lower leg to move from approximately 90 to 160 deg extension. After each contraction the flywheel momentum helped return the lower leg to the 90 deg starting position. An arterial cuff was placed just below the knee in order to ensure that leg blood flow was representative of supply to the active muscles. Static handgrip was performed as handgrip with both arms at 20 % of maximal voluntary contraction (MVC), determined 30 min prior to the experiments. An arterial cuff was placed on both upper arms and inflated to suprasystolic pressure to induce ischaemia in the exercising forearms (see exercise protocol in Table 1).

Table 2. Exercise protocol 2

Arm ischaemia	—	—	—	+	+
Arm work, 20 % MVC	—	+	—	+	—
Minutes	6	6	15	6	3

The study consisted of two 51 min periods with dynamic knee extension performed at 20 and 40 W, respectively. Twenty watts was a very light, and 40 W a moderate, exercise level for all subjects. The subjects exercised according to the protocol in Table 1. In each period there was 6 min of (1) dynamic knee extension, (2) combined dynamic knee extension and static handgrip, or (3) combined knee extension and static handgrip plus forearm ischaemia followed by 3 min of knee extension and post-exercise forearm ischaemia. The order of leg exercise only, leg exercise plus handgrip and leg exercise plus handgrip and forearm muscle ischaemia was randomized. Subjects rested for 15 min between each 6 min exercise period.

In a separate study on four subjects muscle sympathetic nerve activity (MSNA) was measured by microneurography according to the protocol in Table 2. Leg exercise was not performed in this protocol due to the nerve recording, which is very sensitive to even small movements of the leg. We are aware that the experimental conditions in this substudy are not completely identical to the conditions in the main study, but other studies have shown that muscle sympathetic nerve activity does not increase above resting levels during upright dynamic leg exercise at the exercise intensities used in this protocol (Ray *et al.* 1993; Saito & Nakamura, 1995). Thus, baseline MSNA was considered comparable in the two protocols.

Measurements and calculations

Blood pressure was measured via a 20 gauge (1·0 mm) arterial catheter inserted percutaneously into the right femoral artery. The pressure was recorded from Statham P23ID (Costa Mesa, CA, USA) or from Baxter (Uden, The Netherlands) strain gauge pressure transducers connected to a Simonsen and Weel Press 8041 amplifier (Copenhagen, Denmark). Mean arterial pressure was calculated as diastolic pressure + 1/3 of the pulse pressure. Heart rate was continuously monitored from the electrocardiogram.

Cardiac output was determined by dye dilution (Dow, 1956). Five milligrams of Indocyanine Green (Cardio-Green, Becton Dickinson, Franklin Lakes, NJ, USA) in 2 ml of sterile water was injected via a centrally placed venous catheter inserted from the right cubital

Table 3. Cardiovascular and metabolic responses

	Rest	L	L + A	L + A + I	L + I
$[Lactate]_a$ (mmol l^{-1}), rest + 20 W	0·7 ± 0·1	0·8 ± 0·1	0·7 ± 0·1	0·6 ± 0·1	0·7 ± 0·1
$[Lactate]_a$ (mmol l^{-1}), 40 W	—	0·8 ± 0·1	0·9 ± 0·1	0·8 ± 0·1	0·9 ± 0·6
$[Lactate]_v$ (mmol l^{-1}), rest + 20 W	0·7 ± 0·1	0·9 ± 0·1	0·7 ± 0·1	0·7 ± 0·1	0·8 ± 0·1
$[Lactate]_v$ (mmol l^{-1}), 40W	—	1·0 ± 0·1	0·9 ± 0·2	0·9 ± 0·2	1·0 ± 0·7
Leg lactate release (mmol min^{-1}), 20 W	—	0·2 ± 0·2	0·2 ± 0·1	0·3 ± 0·1	0·3 ± 0·1
Leg lactate release (mmol min^{-1}), 40 W	—	0·7 ± 0·3	0·6 ± 0·2	0·6 ± 0·2	0·7 ± 0·7
$[Glucose]_a$ (mmol l^{-1}), rest + 20 W	4·9 ± 0·2	4·7 ± 0·2	4·5 ± 0·2	4·6 ± 0·3	4·5 ± 0·2
$[Glucose]_a$ (mmol l^{-1}), 40 W	—	4·4 ± 0·1	4·4 ± 0·1	4·2 ± 0·1	4·4 ± 0·6
$[Glucose]_v$ (mmol l^{-1}), rest + 20 W	4·3 ± 0·3	4·6 ± 0·2	4·4 ± 0·2	4·4 ± 0·2	4·4 ± 0·2
$[Glucose]_v$ (mmol l^{-1}), 40 W	—	4·2 ± 0·1	3·4 ± 0·7	4·1 ± 0·1	4·2 ± 0·4
Leg glucose uptake (mmol min^{-1}), 20 W	—	0·4 ± 0·4	0·5 ± 0·2	0·8 ± 0·2	0·3 ± 0·4
Leg glucose uptake (mmol min^{-1}), 40 W	—	0·8 ± 0·5	0·6 ± 0·4	0·6 ± 0·1	1·34 ± 1·6
Stroke volume (ml), rest + 20 W	94 ± 7	105 ± 9	108 ± 10	109 ± 11	114 ± 8
Stroke volume (ml), 40 W	—	123 ± 7	135 ± 7	140 ± 10	149 ± 14

a, arterial; v, venous sample. L, leg exercise; L + A, leg plus arm exercise; L + A + I, leg plus arm exercise plus forearm ischaemia; L + I, leg exercise plus post-exercise forearm ischaemia.

vein. Arterial blood was withdrawn from the femoral artery catheter at a rate of 20 ml min^{-1} (Harvard pump model 2202A, Harvard Apparatus Inc., Holliston, MA, USA). A photodensitometer cuvette (DC-410, Waters Instruments Inc., Rochester, MN, USA) was placed between the catheter and the pump and connected to a cardiac output computer (CO-10, Waters Instruments Inc.). The dye dilution curves were recorded on a Gould TA-2000 thermal array recorder (Gould Electronics, Franklin, MA, USA). Withdrawn heparinized blood was re-infused following each determination. Calibration was performed after the experiment using blood samples with dye concentrations of 2·5 and 5 mg l^{-1}, respectively. Cardiac output was measured at the end of each 6 min exercise period.

Leg blood flow was determined by the constant infusion thermodilution technique (Andersen & Saltin, 1985). A 12 cm Teflon 13 gauge (2·3 mm) catheter was inserted percutaneously in the right femoral vein with the tip advanced to a location approximately 2 cm above the inguinal ligament. A thermistor probe (Edslab probe 94-030-2.5F, American Edwards Laboratories, CA, USA) was inserted through the venous catheter and advanced 6–8 cm proximal to the catheter tip. Through four sideholes, ice-cold saline was infused at a rate of 80–120 ml min^{-1} for 15–20 s. Blood temperature was recorded continuously by an Edslab Cardiac Output Computer 9520 (USA). Blood flow measurements were obtained twice during each 6 min exercise period, the first after 4 min of exercise.

Leg vascular conductance was calculated as the mean of the two leg blood flows divided by the mean arterial pressure. Leg oxygen uptake was calculated from the mean of the two leg blood flows and a single determination of arterial and femoral venous oxygen concentration.

Blood samples were taken simultaneously from the femoral artery and vein between the two blood flow measurements in each 6 min period. Haemoglobin content and oxygen saturation were measured on an OSM II Hemoxymeter (Radiometer, Copenhagen, Denmark). Plasma lactate was measured by a YSI 2300 STAT PLUS glucose and L-lactate analyser (Yellow Springs Instruments Co., Yellow Springs, OH, USA). Plasma adrenaline and noradrenaline were measured by high performance liquid chromatography technique (Hewlett Packard 1050, USA).

Muscle sympathetic nerve activity (MSNA) was measured by microneurography. Multiunit recordings were obtained with unipolar tungsten microelectrodes inserted into postganglionic muscle sympathetic nerve fascicles of the right peroneal nerve. MSNA was expressed as (a) the number of bursts of sympathetic activity per minute, and (b) the number of bursts per minute multiplied by the mean burst amplitude in that minute (total activity). For details see Hansen *et al.* (1996).

Values in the text are means ± S.E.M. except when otherwise stated. Friedman's two-way analysis of variance by rank was used to evaluate differences between the experiments and if proven significant, deviating results were located by Wilcoxon's matched pairs signed rank test. The level of significance was set to 0·05.

RESULTS

Blood pressure, heart rate and cardiac output

Mean arterial blood pressure was 88 ± 11 mmHg at rest and 98 ± 11 and 99 ± 10 mmHg during leg exercise at 20 and 40 W, respectively. When static handgrip was added, the mean blood pressure increased to 113 ± 10 mmHg at 20 W ($P = 0·005$) and 112 ± 11 mmHg at 40 W ($P = 0·003$). When static handgrip plus forearm ischaemia was added, the mean blood pressure increased further to 129 ± 9 mmHg at 20 W ($P = 0·005$) and 128 ± 12 mmHg at 40 W ($P = 0·003$). During leg exercise and post-exercise forearm ischaemia (after static handgrip plus forearm ischaemia) the mean blood pressure decreased to 121 ± 16 mmHg at 20 W ($P = 0·04$) and 117 ± 9 mmHg at 40 W ($P = 0·003$) when compared with leg exercise plus static handgrip and forearm ischaemia, but it was still higher than during leg exercise alone at both work rates ($P = 0·005$). There was no difference between the individual blood pressure responses at 20 and 40 W leg exercise (Fig. 1*A*). Blood pressure returned to

control values within 45 s after cessation of vascular occlusion (not shown).

Heart rate was 60 ± 13 beats min^{-1} at rest. During leg exercise heart rate was 76 ± 10 beats min^{-1} at 20 W and increased to 89 ± 13 beats min^{-1} at 40 W ($P = 0{\cdot}005$). When static handgrip was added heart rate increased to 81 ± 8 beats min^{-1} at 20 W ($P = 0{\cdot}05$) and 97 ± 13 beats min^{-1} at 40 W ($P = 0{\cdot}003$). When static handgrip plus forearm ischaemia was added, heart rate was 88 ± 11 beats min^{-1} at 20 W ($P = 0{\cdot}007$) and 103 ± 18 beats min^{-1} at 40 W ($P = 0{\cdot}004$). During leg exercise and post-exercise forearm ischaemia heart rate decreased to 78 ± 10 beats min^{-1} at 20 W ($P = 0{\cdot}01$) and to 94 ± 14 beats min^{-1} at 40 W ($P = 0{\cdot}01$) when compared with leg exercise plus static handgrip and forearm ischaemia. There was no significant difference in heart rate between leg exercise alone and leg exercise plus post-exercise forearm ischaemia (Fig. 1*B*).

Cardiac output was measured in six subjects. Cardiac output was $5{\cdot}9 \pm 1{\cdot}8$ l min^{-1} at rest. During leg exercise cardiac output was $7{\cdot}7 \pm 0{\cdot}5$ l min^{-1} at 20 W and increased to $11{\cdot}0 \pm 2{\cdot}2$ l min^{-1} at 40 W ($P = 0{\cdot}03$). When static handgrip was added, cardiac output was $8{\cdot}6 \pm 1{\cdot}0$ l min^{-1} at 20 W ($P = 0{\cdot}08$) and $12{\cdot}9 \pm 1{\cdot}9$ l min^{-1} at 40 W ($P = 0{\cdot}06$). When static handgrip plus forearm ischaemia was added, cardiac output was $9{\cdot}3 \pm 1{\cdot}8$ l min^{-1} at 20 W ($P < 0{\cdot}05$) and $14{\cdot}0 \pm 3{\cdot}3$ l min^{-1} at 40 W ($P = 0{\cdot}04$). During leg exercise and post-exercise forearm ischaemia, cardiac output was reduced to $8{\cdot}8 \pm 1{\cdot}8$ l min^{-1} at 20 W ($P = 0{\cdot}14$) and $13{\cdot}8 \pm 3{\cdot}9$ l min^{-1} at 40 W ($P = 0{\cdot}06$) (Fig. 1*C*).

Stroke volume was higher during 40 W leg exercise compared with 20 W ($P = 0{\cdot}03$). There was a tendency to an increase in stroke volume with static handgrip with and without forearm ischaemia at 40 W leg exercise, but it did not reach statistical significance ($P = 0{\cdot}06$; Table 3).

Systemic vascular conductance was higher at 40 W compared with 20 W leg exercise ($P = 0{\cdot}03$). There was no significant change in systemic vascular conductance with static handgrip with and without forearm ischaemia or post-exercise forearm ischaemia (Fig. 1*D*).

Leg blood flow and oxygen uptake

During leg exercise leg blood flow was $3{\cdot}6 \pm 0{\cdot}7$ and $5{\cdot}2 \pm 1{\cdot}0$ l min^{-1} at 20 and 40 W, respectively. There was no change in leg blood flow during static handgrip with or without forearm ischaemia or during post-exercise forearm ischaemia (Fig. 2*A*).

Leg vascular conductance was 31 ± 8 and 45 ± 11 ml min^{-1} mmHg^{-1} during leg exercise at 20 and 40 W, respectively ($P = 0{\cdot}005$). There was a tendency to a decrease during static handgrip, but it was not significant. During static handgrip plus forearm ischaemia leg vascular conductance

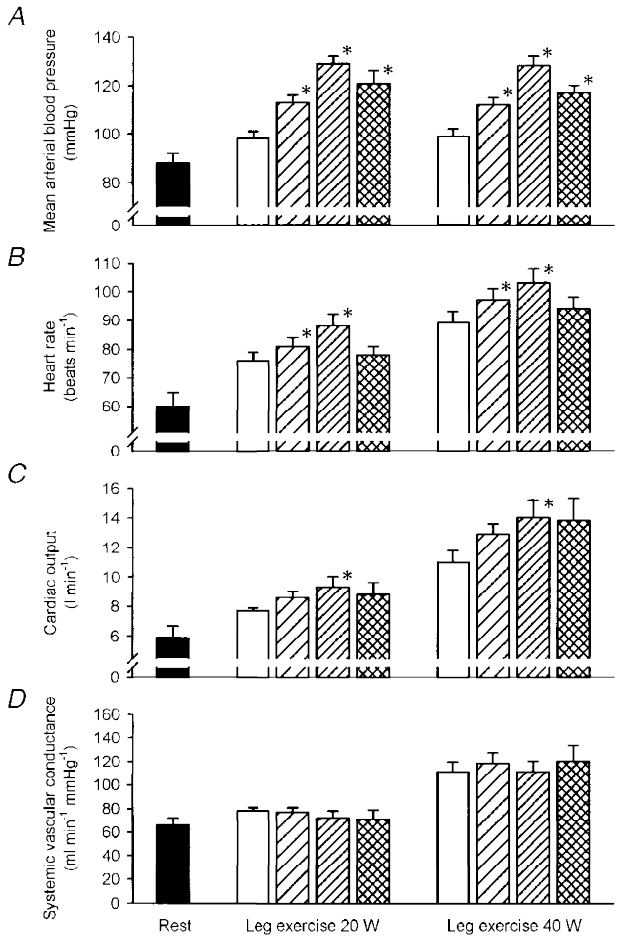

Figure 1

Mean arterial blood pressure (*A*), heart rate (*B*), cardiac output (*C*) and systemic vascular conductance (*D*) at rest and during leg exercise at 20 and 40 W. Values are means ± S.E.M. * Significantly different from control (dynamic leg work only). ■, rest; □, dynamic leg work only; ▨, dynamic leg work plus static handgrip; ▨, dynamic leg work plus static handgrip plus forearm ischaemia; and ▩, dynamic leg work plus post-exercise forearm ischaemia.

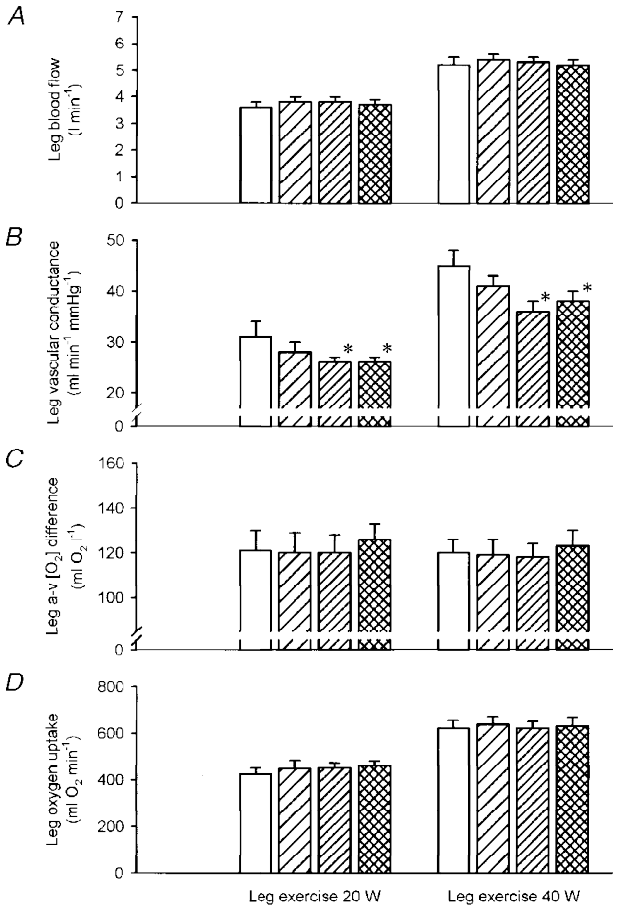

Figure 2
Leg blood flow (*A*), leg vascular conductance (*B*), leg arteriovenous [O_2] difference (*C*) and leg oxygen uptake (*D*) during leg exercise at 20 and 40 W. Values are means ± S.E.M. * Significantly different from control (dynamic leg work only). Symbols as in Fig. 1.

decreased to 26 ± 4 and 36 ± 5 ml min^{-1} $mmHg^{-1}$ at 20 W ($P = 0{\cdot}02$) and 40 W ($P = 0{\cdot}01$), respectively. Post-exercise forearm ischaemia also reduced leg vascular conductance compared with control, to 26 ± 4 and 38 ± 7 ml min^{-1} $mmHg^{-1}$ at 20 W ($P = 0{\cdot}04$) and 40 W ($P = 0{\cdot}03$), respectively (Fig. 2*B*).

Leg arteriovenous oxygen difference was 121 ± 9 and 120 ± 6 ml O_2 l^{-1} and leg oxygen uptake 425 ± 83 and 621 ± 121 ml O_2 min^{-1} at 20 and 40 W, respectively, and there was no change with static handgrip with or without forearm ischaemia or post-exercise forearm ischaemia (Fig. 2*C* and *D*).

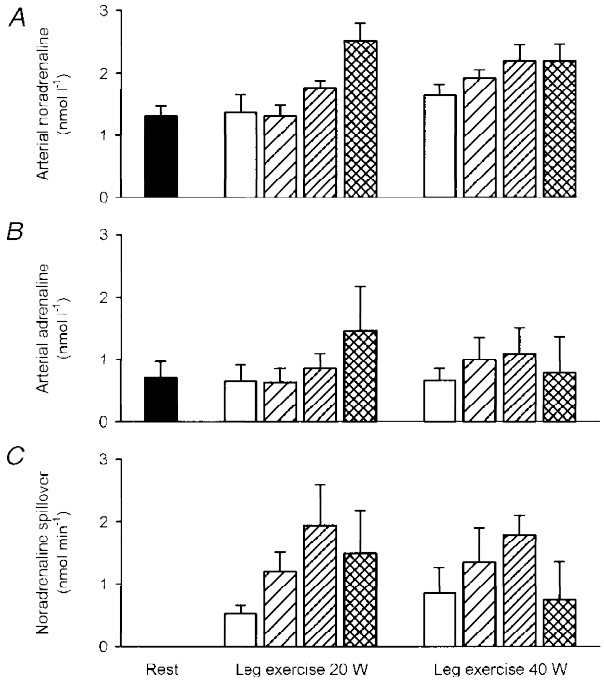

Figure 3
Arterial [noradrenaline] (*A*), [adrenaline] (*B*) and leg noradrenaline spillover (*C*) at rest and during leg exercise at 20 and 40 W. Values are means ± S.E.M. Symbols as in Fig. 1.

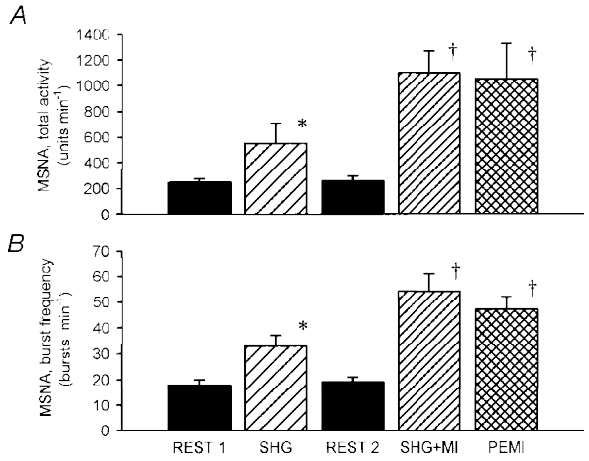

Figure 4

Muscle sympathetic nerve activity expressed as total activity (burst frequency × mean burst amplitude) (*A*) and burst frequency (*B*) (protocol in Table 2). Values are means ± S.E.M. * Significantly different from rest. † Significantly different from static handgrip without forearm muscle ischaemia (SHG). ■, rest; ▨, static handgrip (SHG); ▨, static handgrip plus forearm muscle ischaemia (SHG + MI); ▩, post-exercise forearm muscle ischaemia (PEMI).

Leg noradrenaline spillover, glucose uptake and lactate release

Plasma noradrenaline and adrenaline values were low and did not change significantly from rest with any combination of arm and leg exercise although there was a tendency towards increasing values during static handgrip plus forearm ischaemia and post-exercise forearm ischaemia (Fig. 3). Noradrenaline spillover from the leg also tended to increase with arm exercise with or without forearm ischaemia (Fig. 3).

Arterial glucose and lactate levels as well as leg glucose uptake and lactate release were identical under all exercise conditions (Table 3).

Muscle sympathetic nerve activity

Segments of the original integrated neurogram from one subject are shown in Fig. 5 (last 80 s of the control period and each of the exercise periods). After a latency period of ~1 min, MSNA increased progressively during static handgrip. Averaged over the last 3 min of each intervention, corresponding to the time of the blood flow measurements in protocol 1, total muscle sympathetic nerve activity ($MSNA_{total}$) increased 2-fold during static handgrip and 4-fold during static handgrip plus forearm ischaemia (Fig. 4*A*). During post-exercise forearm ischaemia $MSNA_{total}$ was still high and not different from the level during static handgrip plus forearm ischaemia. MSNA expressed as burst frequency is included in Fig. 4*B*. The relative changes in

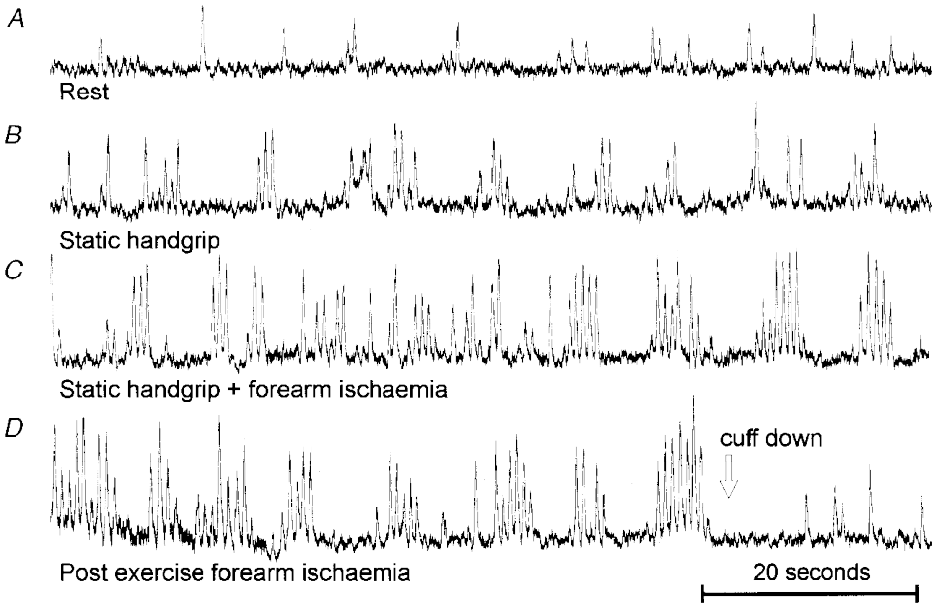

Figure 5. Original nerve recording

Original nerve recording showing the integrated neurogram during the last 80 s of rest (*A*), static handgrip (*B*), static handgrip plus forearm ischaemia (*C*) and post-exercise forearm ischaemia (*D*).

burst frequency were a little lower than the changes in total activity (burst frequency × mean burst amplitude), but the pattern was similar.

DISCUSSION

In this study activation of a powerful exercise pressor reflex by static ischaemic arm exercise, causing a 4-fold increase in muscle sympathetic vasoconstrictor activity did not affect blood flow or oxygen delivery to the knee extensor muscles exercising at a low and moderate intensity. However, leg vascular conductance was reduced in line with the higher perfusion pressure resulting from a 15–32% increase in mean arterial pressure during concomitant arm work.

These observations are in agreement with the findings of Kilbom & Brundin (1976) but differ from those of Kagaya (1993) and Kagaya *et al.* (1994) who saw a reduction in calf blood flow during simultaneous dynamic plantar flexion and static handgrip. The major differences between the present study and the studies by Kagaya (1993) and Kagaya *et al.* (1994) are (1) the larger muscle mass, longer exercise duration, and the higher work rate of the dynamically exercising muscles in the present study, (2) the power of the exercise pressor reflex, and (3) the method used for muscle blood flow measurement. In the study by Kagaya *et al.* (1994) dynamic exercise was confined to rhythmic plantarflexion of the foot at a very low exercise intensity (10% maximum voluntary contraction, MVC). The power of the exercise pressor reflex associated with the arm work in the present study is comparable with or higher than that in the study by Kagaya *et al.* (1994). Kagaya *et al.* (1994) used static handgrip with one arm at 50% MVC for 51 s resulting in a 2-fold increase in MSNA burst frequency (2 subjects). In the present study static handgrip with both arms at 20% MVC with or without occlusion of forearm blood supply was applied for 6 min, resulting in a 2-fold (handgrip) and 3-fold (handgrip plus forearm ischaemia) increase in burst frequency (2- and 4-fold increase in total activity, respectively). In this context it should also be noted that in the study by Kagaya *et al.* (1994) muscle blood flow was measured after exercise had ceased (venous occlusion plethysmography). It has been demonstrated that rapid changes in blood flow and muscle oxygenation take place as soon as exercise ceases and therefore measurements made at this time do not necessarily bear a close relation to the conditions during exercise (Wade & Bishop, 1962; Hansen *et al.* 1996). Several other studies addressing the same question have similar drawbacks in using venous occlusion plethysmography for muscle blood flow measurement (Strandell & Shepherd, 1967; Joyner *et al.* 1990; Sinoway & Prophet, 1990).

Leg vascular conductance was reduced during static handgrip plus forearm ischaemia and during post-exercise forearm ischaemia at both leg work rates. In contrast to previous findings (Kilbom & Brundin, 1976; Kagaya, 1993; Kagaya *et al.* 1994) there was only a tendency to a reduction in leg vascular conductance during static handgrip without forearm ischaemia. Whether the observed reduction in muscle vascular conductance indicates sympathetic vasoconstriction in the active leg muscles or whether it is simply the result of metabolic autoregulation of muscle blood flow is still a matter of controversy. Concomitant static ischaemic arm exercise and dynamic leg exercise will increase blood pressure and sympathetic vasoconstrictor activity to the leg muscles due to a metabolic reflex arising in the exercising ischaemic arm muscles. If the leg muscle vascular bed was totally passive, leg muscle blood flow would increase in response to the higher perfusion pressure. However, leg muscle blood flow is unaffected by this manoeuvre, indicating that either the increased sympathetic vasoconstrictor activity associated with the arm exercise prevented the increase in leg muscle blood flow or that local metabolic autoregulation in the exercising leg muscles prevented hyperperfusion (initial leg muscle hyperperfusion associated with the increase in blood pressure would decrease the metabolic 'error' signal in the muscles leading to a gradual decrease in vascular dilatation).

Blood pressure increased above control (leg exercise only) by 15% during static handgrip, 29–32% during static handgrip plus forearm ischaemia and 18–23% during post-exercise forearm ischaemia. These differences illustrate the importance of the metaboreflex for the blood pressure response to this type of exercise but also emphasize the contribution of central command during exhaustive exercise. In accordance with this are the findings by Leonard *et al.* (1985) and Mitchell *et al.* (1989), who demonstrated the importance of both metaboreflexes and central command for the blood pressure response to static exercise. The increments in arterial blood pressure were similar during arm interventions at 20 and 40 W leg exercise. This is in accordance with Kilbom & Brundin (1976) who also found similar increases in blood pressure during static handgrip at rest and in combination with dynamic leg exercise.

Cardiac output tended to increase with static handgrip (P values were slightly above 0·05) and was significantly higher during static handgrip plus forearm ischaemia ($P = 0{\cdot}04$). During post-exercise forearm ischaemia cardiac output also tended to be higher ($P = 0{\cdot}14$ and 0·06 at 20 and 40 W, respectively). Stroke volume was higher during 40 W leg exercise compared with 20 W, but did not change significantly with forearm exercise or ischaemia. Thus, the increase in cardiac output could mainly be attributed to the increase in heart rate. Systemic vascular conductance did not change with forearm exercise or ischaemia. These findings are in accordance with a number of previous studies demonstrating a major contribution of cardiac output to the exercise pressure response (Shepherd *et al.* 1981) and pressure response to post-exercise muscle ischaemia (Bonde Petersen *et al.* 1978).

Despite a pronounced increase in muscle sympathetic nerve activity arterial noradrenaline concentrations and leg noradrenaline spillover were only slightly elevated during arm exercise and post-exercise forearm ischaemia. This discrepancy is consistent with previous findings of a 2- to 4-fold greater increase in muscle sympathetic nerve activity compared with plasma noradrenaline during static exercise (Wallin *et al.* 1981).

In conclusion, activation of a powerful exercise pressor reflex by static ischaemic arm exercise, causing a 4-fold increase in muscle sympathetic nerve activity did not affect blood flow to the knee extensor muscles exercising at a low and moderate intensity. Muscle vascular conductance was significantly reduced, and the question remaining to be answered is whether this is due to vasoconstrictor activity in the active muscles or metabolic autoregulation of muscle blood flow.

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